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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
LEE,L	

ART UNIT	PAPER NUMBER
1645	7

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/150,947	Applicant(s) Kaempfer
	Examiner Li Lee	Group Art Unit 1645

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-49* is/are pending in the application.

Of the above, claim(s) *34-39 and 41-49* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-33 and 40* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Election/Restrictions

I. Claims 1-33, and 40, drawn to a peptide comprising an amino acid sequence substantially homologous to the amino acid sequence of a pyrogenic exotoxin and a vaccine, classified in class 530, subclass 350.

II. Claims 34-39, drawn to a method for treating, preventing, or conferring immunity harmful effects and toxic shock induced by pyrogenic exotoxin by administering the peptide, classified in class 514, subclass 12.

III. Claims 41-46, drawn to an antibody, classified in class 530, subclass 350.

IV. Claims 47-49, drawn to a method for assessing the efficacy of a vaccination and a kit for assessing the efficacy of a vaccination, classified in class 435, subclass 7.1.

1. The inventions are distinct, each from the other because of the following reasons:

Groups I and III are drawn to different products. The claims of Group I are drawn to a polypeptide capable of eliciting protective immunity against toxic shock induced by a pyrogenic exotoxin, those of Group II are drawn to an antibody. The inventions can be shown to be distinct because they are made by different methods and because they are physically and functionally distinct chemical entities.

Inventions groups I and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the

product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the polypeptide of Group I can be used in a materially different process, such as in vitro assay of antibody or purifying antibodies.

Inventions I and IV are independent and distinct, wherein the polypeptide of Group I can be neither made nor used in the method of Invention IV.

Inventions II and III or IV are independent and distinct, wherein the antibody of Group II can be neither made nor used in the methods of Invention III or IV.

During a telephone conversation with Ronald Hildreth on 8/26/99 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-33, and 40. Affirmation of this election must be made by applicant in replying to this Office action. Claims 34-39 and 41-49 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Drawings

2. This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings are objected to by the draftsperson under 37 C.F.R. 1.84 or 1.152. See PTO-948 for details. Correction of the noted defects can be deferred until the application is allowed by the examiner.

Specification

3. The abstract of the disclosure is objected to because it contains more than one paragraph. Correction is required. See MPEP § 608.01(b).

Claim Objections

4. Claim 40 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 40 is a dependent claim which refers to two claims in the conjunctive ("1" and "30" or "2" and "27") rather than in the alternative ("1" or "30", or "2" or "27"). Accordingly, the claim 40 is not been further treated on the merits.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 1-33 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The claims are drawn to a peptide comprising an amino acid sequence, which reads on a product of nature. The claims should be amended to indicate the hand of the man. See MPEP 2105.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantially homologous" in claims 1-33 is a relative term which renders the claim indefinite. The term "substantially homologous" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and in the absence of a clear recitation of the specific algorithm and specific parameters employed for comparison of amino acid sequences, one of the ordinary skill in the art would not be reasonably be apprised of the metes and bounds of the claimed subject matter.

Claim 23 recites the limitation "the corresponding position". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-8, 13-16, 18, 21, 23, 26-30 are rejected under 35 U.S.C. 102(b) as being anticipated by Tseng et al (Infection and Immunity 63 (8):2880-2885, Aug 1995).

Claims 1-8, 13-16, 18, 21, 23, 26-30 are drawn to a peptide in the multimer and chemical modification and derivatives of said peptide/a pharmaceutical composition /a vaccine, comprising an amino acid sequence substantially homologous to the amino acid sequence of a fragment of *Staphylococcus aureus* enterotoxin B (SEB), wherein the peptide comprising the amino acid sequence is shown in SEQ ID Nos 1, 4, or 5, capable of eliciting protective immunity against toxic shock induced by a pyrogenic exotoxic or by a mixture of pyrogenic exotoxins, and capable of inhibiting expression of pyrogenic toxin-induced mRNA encoded by the IL-2, IFN-γ or TNF-β genes, or capable of eliciting the production of antibodies that block T-cell activation, or capable of antagonizing toxin-mediated activation of T cells.

Tseng et al teach that a peptide in the multimer (*Staphylococcus aureus* enterotoxin B (SEB) containing microspheres) and chemical modification (precipitated with alum) and derivatives of said peptide/a pharmaceutical composition /a vaccine comprises the amino acid sequence SEQ ID Nos 1, 4, and 5 which is comprised in the naturally occurred *Staphylococcus aureus* enterotoxin B (SEB) (see Huang et al J Biol Chem 245 (14) :3518-3525, 1970, page 3523) and is capable of eliciting protective immunity against toxic shock induced by a pyrogenic exotoxin and by a mixture of pyrogenic exotoxins, and capable of inhibiting expression of pyrogenic toxin-induced mRNA encoded by the IL-2, IFN-γ or TNF-β genes, capable of eliciting the production of antibodies that block T-cell activation, and capable of antagonizing toxin-mediated activation of T cells because the protective immunity is correlate with anti-SEB antibodies which seemed to neutralize the SEB (see Abstract and Material and Methods). The art teaches that SEB is a superantigen which is associated with toxic shock syndrome and activating both T cells and antigen presenting cells resulting in a massive production of cytokines and mediators including IL-2, IFN-γ or TNF-β, which then cause the disease (Lowell et al. Infection and Immunity 64 (5):1706-1713, May 1996). Therefore, the neutralization of SEB protects the host free from the disease caused by the superantigen associated malfunction activities. Thus, Tseng et al meet the limitations of the claims.

11. Claims 1-8, 13-16, 18, 21, 23, 26-33 are rejected under 35 U.S.C. 102(b) as being anticipated by Lowell et al (Infection and Immunity 64 (5):1706-1713, May 1996).

Claims 1-8, 13-16, 18, 21, 23, 26-33 are drawn to a peptide in the multimer and chemical modification and derivatives of said peptide/a pharmaceutical composition /a vaccine comprising a adjuvant combination of proteosomes and alum for enhancing production of antibodies that block T cell activation, comprising an amino acid sequence substantially homologous to the amino acid sequence of a fragment of *Staphylococcus aureus* enterotoxin B (SEB), wherein the peptide comprising the amino acid sequence is shown in SEQ ID Nos 1, 4, or 5, capable of eliciting protective immunity against toxic shock induced by a pyrogenic exotoxic or by a mixture of pyrogenic exotoxins, and capable of inhibiting expression of pyrogenic toxin-induced mRNA encoded by the IL-2, IFN-γ or TNF-β genes, or capable of eliciting the production of antibodies that block T-cell activation, or capable of antagonizing toxin-mediated activation of T cells.

Lowell et al teach that a peptide (*Staphylococcus aureus* enterotoxin B (SEB)) in the multimer (formulation of SEB toxoid with proteosomes, greater than 90% polymeric, see Material and Methods, and Discussion) and chemical modification (treated with formalin, see Material and Methods) and derivatives of said peptide/a pharmaceutical composition /a vaccine comprising a adjuvant combination of proteosomes and alum for enhancing production of antibodies that block T cell activation comprises the amino acid sequence SEQ ID Nos 1, 4, and 5 which is comprised in the naturally occurred *Staphylococcus aureus* enterotoxin B (SEB) (see Huang et al J Biol Chem 245 (14) :3518-3525, 1970, page 3523) and is capable of eliciting protective immunity against toxic shock induced by a pyrogenic exotoxin and by a mixture of pyrogenic exotoxins, and capable of inhibiting expression of pyrogenic toxin-induced mRNA

encoded by the IL-2, IFN-γ or TNF-β genes, capable of eliciting the production of antibodies that block T-cell activation, and capable of antagonizing toxin-mediated activation of T cells since the protective immunity is correlate with neutralizing antibodies against SEB (see Abstract and Material and Methods).The art teaches that SEB is a superantigen which is associated with toxic shock syndrome and activating both T cells and antigen presenting cells resulting in a massive production of cytokines and mediators including IL-2, IFN-γ or TNF-β, which then cause the disease (Lowell et al. Infection and Immunity 64 (5):1706-1713, May 1996). Therefore, the neutralization of SEB protects the host free from the disease caused by the superantigen associated malfunction activities. Thus, Lowell et al meet the limitations of the claims.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1-8, 13-16, 18, 21, 23, 26-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lowell et al (Infection and Immunity 64 (5):1706-1713, May 1996) and Tamura et al (US Patent 5,310,874, May 10, 1994).

Claims 1-8, 13-16, 18, 21, 23, 26-33 are drawn to a peptide in the multimer and chemical modification and derivatives of said peptide/a pharmaceutical composition /a vaccine comprising a adjuvant combination of KLH and alum for enhancing production of antibodies that block T cell activation, comprising an amino acid sequence substantially homologous to the amino acid sequence of a fragment of *Staphylococcus aureus* enterotoxin B (SEB), wherein the peptide is shown in SEQ ID Nos 1, 4, or 5 which is a fragment of natural SEB (see Specification of page 56, Table 4), capable of eliciting protective immunity against toxic shock induced by a pyrogenic exotoxic or by a mixture of pyrogenic exotoxins, and capable of inhibiting expression of pyrogenic toxin-induced mRNA encoded by the IL-2, IFN-γ or TNF-β genes, or capable of eliciting the production of antibodies that block T-cell activation, or capable of antagonizing toxin-mediated activation of T cells.

Lowell et al teach that a peptide (*Staphylococcus aureus* enterotoxin B (SEB)) in the multimer (formulation of SEB toxoid with proteosomes, greater than 90% polymeric, see Material and Methods, and Discussion) and chemical modification (treated with formalin, see Material and Methods) and derivatives of said peptide/a pharmaceutical composition /a vaccine comprising a adjuvant combination of proteosomes and alum for enhancing production of antibodies that block T cell activation have the amino acid sequence SEQ ID Nos 1, 4, and 5 which is comprised in the naturally occurred *Staphylococcus aureus* enterotoxin B (SEB) (see Huang et al J Biol Chem 245 (14) :3518-3525, 1970, page 3523) and is capable of eliciting protective immunity against toxic shock induced by a pyrogenic exotoxic or by a mixture of

pyrogenic exotoxins, and capable of inhibiting expression of pyrogenic toxin-induced mRNA encoded by the IL-2, IFN-γ or TNF-β genes, or capable of eliciting the production of antibodies that block T-cell activation, or capable of antagonizing toxin-mediated activation of T cells since the protective immunity is correlate with neutralizing antibodies against SEB (see Abstract and Material and Methods).The art teaches that SEB is a superantigen which is associated with toxic shock syndrome and activating both T cells and antigen presenting cells resulting in a massive production of cytokines and mediators including IL-2, IFN-γ or TNF-β, which then cause the disease (Lowell et al. Infection and Immunity 64 (5):1706-1713, May 1996). Therefore, the neutralization of SEB protects the host free from the disease caused by the superantigen associated malfunction activities.

Lowell et al does not teach a vaccine comprising a adjuvant combination of KLH and alum for enhancing production of antibodies that block T cell activation.

However, Tamura et al. teach a vaccine comprising a adjuvant combination of KLH and alum for enhancing production of antibodies (column 23, lines 10-66).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to immunize SEB of Lowell et al with the adjuvant combination of KLH and alum of Tamura because the known benefit of enhancing production of antibodies.

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Status of Claims

14. No claims are allowed. All claims stand rejected. Claims 9-12, 17, 19-20, 22, 24-25 are free from prior art.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1645 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Li Lee, M.D., Ph.D. whose telephone number is (703) 308-8891. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995.

Li Lee, M.D., Ph.D.
September 9, 1999

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